

CHA₂DS₂-VASc and R₂-CHA₂DS₂-VASc scores predict in-hospital and post-discharge outcome in patients with myocardial infarction

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Abstract

Introduction: The CHA₂DS₂-VASc and R₂-CHA₂DS₂-VASc scores were initially designed to evaluate the risk of cerebrovascular events in patients with atrial fibrillation. However, these scales consist of parameters which are well known as general risk factors for cardiovascular events.

Aim: To assess the role of the CHA₂DS₂-VASc and R₂-CHA₂DS₂-VASc scores in predicting outcome of patients with myocardial infarction (MI).

Material and methods: We enrolled 212 consecutive patients with both ST-elevation and non-ST-elevation MI referred for primary percutaneous coronary intervention (PCI). Patients were divided into two groups depending on the CHA₂DS₂-VASc score: ≤ 3 (low score) and > 3 points (high score).

Results: The group with a CHA₂DS₂-VASc score > 3 points consisted of 93 (44%) patients. Follow-up was available in 200 (94.3%) patients with median duration of 10 (Q1: 6; Q3: 13) months. During the follow-up all-cause mortality was greater in patients from the high score group (21%) compared to patients with lower scores (8%) (*p* = 0.009). Recurrent MI was found in 4% of patients from the low score group and in 13% of patients from the high score group (*p* = 0.024). The combined endpoint of cardiovascular mortality, recurrent non-fatal MI and non-fatal stroke occurred in 13% of lower score patients and in 30% of patients with a score > 3 points (*p* = 0.002). In a Cox regression model both scores were predictors of all-cause mortality with a hazard ratio of 1.31 per 1 point increase for the CHA₂DS₂-VASc score (*p* = 0.004) and 1.36 for the R₂-CHA₂DS₂-VASc score (*p* < 0.001).

Conclusions: The CHA₂DS₂-VASc and R₂-CHA₂DS₂-VASc scores predict in-hospital and post-discharge outcome in patients with acute MI undergoing primary PCI.

Key words: acute coronary syndrome, risk, mortality.

Summary

In the present study we demonstrate that simple assessment with the CHA₂DS₂-VASc score predicts outcome in patients with acute myocardial infarction. In receiver-operating characteristics analysis, we established a cut-off value of 3 points for the CHA₂DS₂-VASc score for predicting clinical events during follow-up. Patients with CHA₂DS₂-VASc > 3 had higher rates of all-cause mortality, re-infarction and combined endpoint (cardiovascular death, re-infarction and stroke). Presence of heart failure was associated with the highest hazard ratio for predicting all-cause mortality. Additional renal function assessment (R₂-CHA₂DS₂-VASc score) was associated with an increase in the predictive value for all-cause mortality.

Introduction

Risk assessment is crucial in the decision-making process in patients with cardiovascular diseases. Identification of high-risk individuals allows one to implement

tailored aggressive therapy and improve their outcome. The CHA₂DS₂-VASc was originally designed and validated for evaluating the probability of cerebrovascular events in patients with atrial fibrillation (AF) [1–6]. It is simple and broadly used in clinical practice due to the growing

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number of patients with AF. However, the CHA₂DS₂-VASc score consists of several parameters, namely heart failure, age, gender, history of arterial hypertension, diabetes mellitus, vascular disease and stroke, which are well-known predictors of cardiovascular events [2]. The R₂-CHA₂DS₂-VASc scale also includes renal function assessment [4]. A correlation between higher CHA₂DS₂-VASc score and increased mortality of patients with myocardial infarction (MI) has been found in several analyses [7, 8]. However, the impact of this scale on in-hospital outcome and rates of recurrent MI in patients hospitalized with acute MI remains unclear.

Aim

To assess the value of CHA₂DS₂-VASc and R₂-CHA₂DS₂-VASc scores as predictors of outcome in patients with acute MI.

Material and methods

Study population

The present study is a retrospective analysis of consecutive patients diagnosed with MI who underwent primary percutaneous coronary intervention (PCI) in a single center. Both ST-segment elevation and non-ST-segment elevation MI patients were included. For better homogeneity of the study group we excluded patients: with MI who were not referred to coronary angiography, with MI with non-obstructive coronary arteries and patients referred for coronary artery bypass grafting. The study was approved by the institutional ethical board. The CHA₂DS₂-VASc score was calculated for all patients regardless of presence of AF by adding 1 point each for presence of congestive heart failure, history of arterial hypertension, diabetes, vascular disease, age ≥ 65 years, female gender, and 2 points each for age ≥ 75 years and history of stroke or transient ischemic attack (TIA). The R₂-CHA₂DS₂-VASc score was assessed by adding 2 extra points for renal function impairment, which was defined by glomerular filtration rate (GFR) ≤ 60 ml/min/1.73 m² calculated with the MDRD formula [4]. History of arterial hypertension, diabetes, vascular disease and stroke was assessed via the patient's medical records. Vascular disease included previous MI, peripheral artery disease or aortic plaque. Congestive heart failure was defined as left ventricular ejection fraction (LVEF) $< 40\%$, measured by echocardiography with signs and symptoms of right or left ventricle failure [1].

Follow-up data were obtained from telephone interviews and medical records in the hospital electronic database. The rates of all-cause and cardiovascular death, recurrent MI and stroke were assessed. Cardiovascular mortality included death resulting from acute MI, stent thrombosis, heart failure, stroke, cardiovascular procedures, sudden cardiac death or other known cardiovascular causes. Combined endpoint was defined as a combi-

nation of cardiovascular mortality, non-fatal recurrent MI and non-fatal stroke. Non-fatal MI and non-fatal stroke were defined as events with survival until hospital discharge. Long-term analysis of clinical events also included those which occurred during the in-hospital course.

Patients' characteristics and rates of clinical events were analyzed in relation to CHA₂DS₂-VASc and R₂-CHA₂DS₂-VASc score categories with cut-off values established by evaluating the area under the curve (AUC) in receiver-operating characteristics analysis (ROC).

Statistical analysis

Quantitative variables were described using means with standard deviation (for normal distribution of data) or median with interquartile range (for non-normal distribution of data). Categorical variables were presented with counts and as percentages. The Mann-Whitney *U* test (for non-normal distribution of data) was applied for continuous variables. The χ^2 test was used for categorical (nominal and dichotomous) variables. Survival was estimated using the Kaplan-Meier method according to CHA₂DS₂-VASc and R₂-CHA₂DS₂-VASc score categories with the log-rank test for full follow-up time available. Adequacy of CHA₂DS₂-VASc and R₂-CHA₂DS₂-VASc scores for predicting clinical outcome was assessed in ROC analysis for full follow-up time available. Univariate and multivariate Cox regression models were used to investigate the effect of each component of the scores for predicting all-cause mortality. The level of statistical significance was set at an α value < 0.05 . All analyses were performed with SPSS Statistics 24 (IBM, Inc. NY, USA).

Results

Study population and in-hospital characteristics

A total of 212 consecutive patients with MI, who underwent primary PCI between September 2016 and July 2017, entered the study. The median CHA₂DS₂-VASc score was 3 (Q1: 2; Q3: 4.5) points. For the R₂-CHA₂DS₂-VASc score the median value was 4 (Q1: 2; Q3: 6). The group with a high CHA₂DS₂-VASc score (> 3) consisted of 93 (44%) patients, whereas a CHA₂DS₂-VASc score ≤ 3 points was found in the remaining 119 (56%) patients. Baseline clinical characteristics are shown in Table I. There were no significant differences in the type of MI (ST-elevation and non-ST-elevation) between groups. Patients with a high CHA₂DS₂-VASc score were by definition older and more often had a history of diabetes mellitus, arterial hypertension, vascular disease, heart failure and stroke. During hospital stay, patients from the high score group more often had respiratory tract infections and required systemic antibiotics. It resulted in longer hospitalization duration and more frequent transfers to general medicine units for treatment continuation. Administration of loop diuretics and aldosterone antagonists was also more

Table I. Baseline and in-hospital course characteristics

Parameter	All patients (n = 212)	CHA ₂ DS ₂ -VASC ≤ 3 (n = 119)	CHA ₂ DS ₂ -VASC > 3 (n = 93)	P-value
Age [years]*	67 ±12	61 (Q1: 56; Q3: 68)	76 (Q1: 69; Q3: 83)	< 0.001
Male gender*	141 (66%)	95 (80%)	46 (49%)	< 0.001
LVEF (%)*	48 (Q1: 40; Q3: 55)	52 (Q1: 45; Q3: 60)	40 (Q1: 33; Q3: 50)	< 0.001
Arterial hypertension*	167 (79%)	81 (68%)	86 (92%)	< 0.001
Vascular disease*	87 (41%)	31 (26%)	56 (60%)	< 0.001
Stroke history*	18 (8%)	1 (1%)	17 (18%)	< 0.001
Diabetes*	77 (36%)	26 (22%)	51 (55%)	< 0.001
ST-segment elevation MI	65 (31%)	37 (31%)	28 (30%)	1.0
Culprit in LAD	78 (37%)	42 (35%)	36 (39%)	0.67
Multi-vessel PCI	76 (36%)	46 (39%)	30 (32%)	0.39
Staged revascularization	46 (22%)	30 (25%)	16 (17%)	0.18
Baseline serum creatinine [μmol/l]	83 (Q1: 69; Q3: 107)	75 (Q1: 67; Q3: 88)	95 (Q1: 76; Q3: 132)	< 0.001
GFR ≤ 60 ml/min/1.73 m ²	64 (30%)	16 (13%)	48 (52%)	< 0.001
AF (history of and new onset)	37 (17%)	11 (9%)	26 (28%)	0.001
ACEI/ARB	171 (81%)	101 (86%)	70 (75%)	0.05
β-Blockers	173 (82%)	100 (85%)	73 (78%)	0.2
Statins	204 (96%)	114 (97%)	90 (97%)	1.0
Loop diuretics	79 (37%)	23 (20%)	56 (60%)	< 0.001
Aldosterone antagonists	46 (22%)	10 (8%)	36 (39%)	< 0.001
RBC transfusion	8 (4%)	4 (3%)	4 (4%)	0.73
Ventricular arrhythmia	17 (8%)	8 (7%)	9 (10%)	0.45
Hospitalization length [days]	7 (Q: 5; Q3: 9)	7 (Q1: 5; Q3: 8)	8 (Q1: 6; Q3: 11)	0.002
Respiratory tract infection	33 (16%)	8 (7%)	25 (27%)	< 0.001
Treatment continuation in an internal medicine unit	12 (6%)	1 (1%)	11 (12%)	0.001

LVEF – left ventricular ejection fraction, MI – myocardial infarction, LAD – left anterior descending artery, PCI – percutaneous coronary intervention, GFR – glomerular filtration rate, AF – atrial fibrillation, ACEI – angiotensin converting enzyme inhibitors, ARB – angiotensin receptor blocker, RBC – red blood cell; *parameters included in the CHA₂DS₂-VASC score.

frequent in those patients. In our analysis baseline GFR was significantly lower in patients with a CHA₂DS₂-VASC score > 3. Atrial fibrillation (including both past medical history and new onset during hospitalization) was more frequent in patients from the high score group (Table I). In patients with a CHA₂DS₂-VASC score > 3, higher in-hospital mortality was observed, but without statistical significance. No cases of recurrent MI were reported during index hospitalization in both groups (Table II).

Long-term clinical outcome

Follow-up was obtained in 200 (94.3%) patients. Median duration of follow-up was 10 (Q1: 6; Q3: 13) months. Follow-up data were not available in 6% of pa-

tients from the low score group and in 5% of patients with a higher score value ($p = 1$). In Table II we show rates of events occurring during follow-up observation (presented as the sum of events occurring during index hospitalization and follow-up). All-cause mortality was significantly greater in patients from the high score group (21%) compared to patients with lower scores (8%) ($p = 0.009$). There was also higher cardiovascular mortality in patients with CHA₂DS₂-VASC > 3 points (15% compared to 8%), although without statistical significance ($p = 0.19$). Among 8 patients from the high score group, who died after index hospitalization, 2 patients died due to cardiovascular causes (recurrent MI and heart failure), 2 patients died from cancer disease and in the remain-

Table II. In-hospital and long-term outcome

Parameter	CHA ₂ DS ₂ -VASc ≤ 3 (n = 119)	CHA ₂ DS ₂ -VASc > 3 (n = 93)	P-value
In-hospital outcome:			
All-cause mortality	10 (8%)	12 (13%)	0.36
Cardiovascular mortality	10 (8%)	12 (13%)	0.36
All recurrent MI	0	0	
Non-fatal recurrent MI	0	0	
All stroke	0	4 (4%)	0.036
Non-fatal stroke	0	2 (2%)	0.19
Combined endpoint	10 (8%)	14 (15%)	0.19
Stent thrombosis	0	0	
Long-term outcome:			
All-cause mortality	10 (8%)	20 (21%)	0.009
Cardiovascular mortality	10 (8%)	14 (15%)	0.19
All recurrent MI	5 (4%)	12 (13%)	0.024
Non-fatal recurrent MI	5 (4%)	11 (12%)	0.064
All stroke	(1%)	5 (5%)	0.09
Non-fatal stroke	(1%)	3 (3%)	0.32
Combined endpoint	15 (13%)	28 (30%)	0.002
Stent thrombosis	0	1 (1%)	0.44

MI – myocardial infarction.

ing 4 patients we could not establish the exact cause of death in a telephone interview and these cases were treated as non-cardiovascular deaths. Recurrent MI was found in 4% of patients from the low score group and in 13% of patients from the high score group ($p = 0.024$). The combined endpoint occurred in 13% of patients with low scores and in 30% of patients with a score > 3 points ($p = 0.002$). Kaplan-Meier survival analysis showed significant differences for all-cause mortality, recurrent MI and combined endpoint between patients with higher and lower CHA₂DS₂-VASc and the R₂-CHA₂DS₂-VASc scores (Figure 1). In a Cox regression model both scores were significant predictors of all-cause mortality with a hazard ratio of 1.31 per 1 point increase for the CHA₂DS₂-VASc score (95% CI: 1.1–1.6, $p = 0.004$) and 1.36 for the R₂-CHA₂DS₂-VASc score (95% CI: 1.2–1.6, $p < 0.001$). In Table III we present the effect of each component of the scores on all-cause mortality. In multivariate analysis of R₂-CHA₂DS₂-VASc score components, heart failure and renal insufficiency were significant predictors of all-cause mortality. In multivariate analysis of CHA₂DS₂-VASc score components only the occurrence of heart failure was a significant predictor of all-cause mortality. Congestive heart failure was associated with the highest hazard ratio, both in an unadjusted and adjusted Cox regression

model. In Table IV and Figure 2 we show ROC analysis for CHA₂DS₂-VASc and R₂-CHA₂DS₂-VASc scores with cut-off values for both scales for predicting clinical events. The R₂-CHA₂DS₂-VASc presented a fair value (AUC > 0.7) for predicting all-cause and cardiovascular mortality and the combined endpoint, whereas the CHA₂DS₂-VASc presented AUC values < 0.7 for predicting clinical events.

Discussion

The major finding of our study is that even simplified evaluation with the CHA₂DS₂-VASc scale could identify patients with acute MI at a higher risk of worse clinical outcome. At the same time, patients with a low CHA₂DS₂-VASc score had a good outcome with a relatively small number of events after discharge.

Early risk stratification helps clinicians in defining a patient's prognosis and managing the treatment strategy. Several scales have been developed to identify high-risk patients who may benefit most from early aggressive therapies, including the Global Registry of Acute Coronary Events, Thrombolysis in Myocardial Infarction, and Primary Angioplasty in Myocardial Infarction [9–12]. However, these scales are complex and require special online calculators. They are well validated in clinical trials but rarely used in everyday clinical practice. The

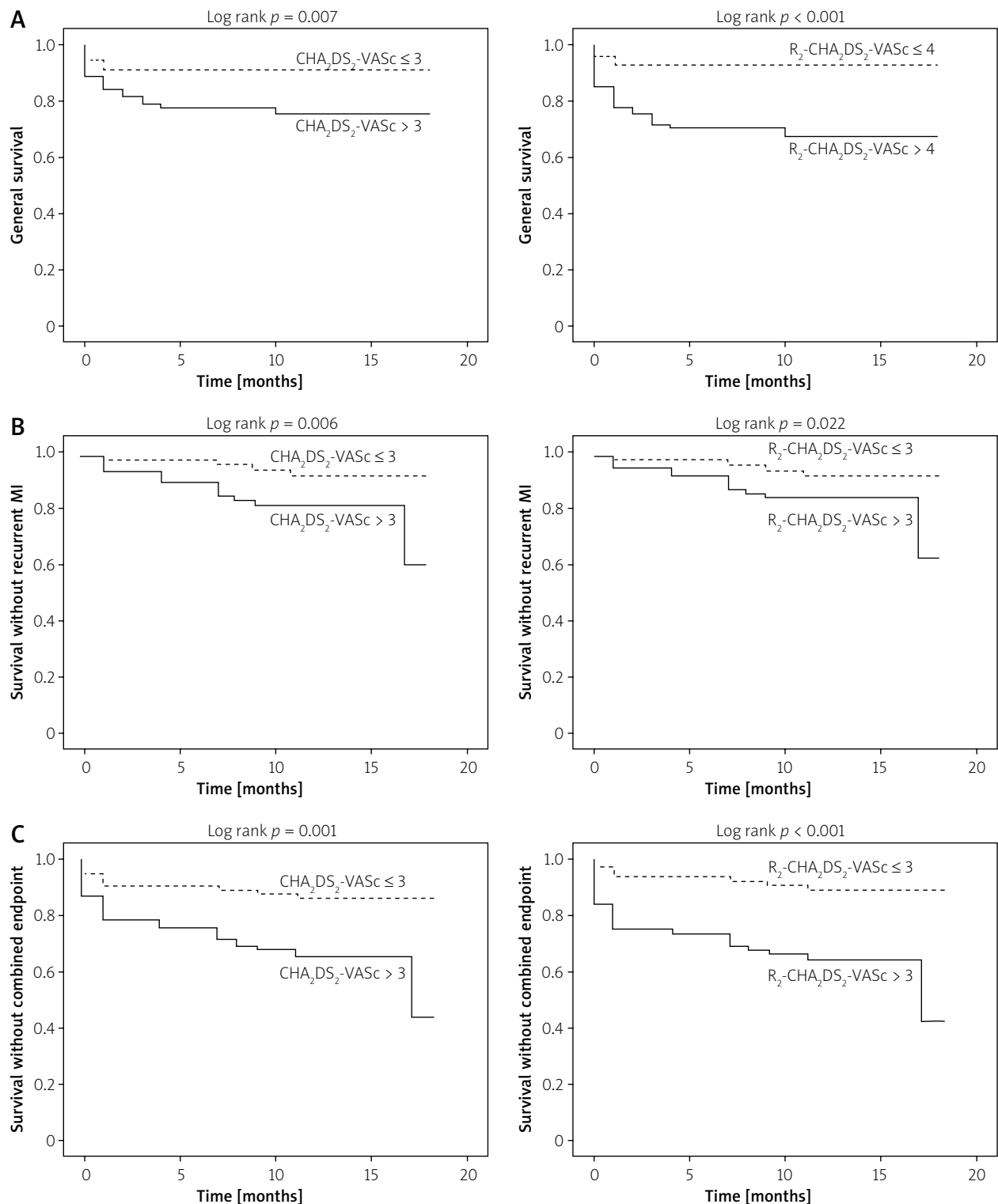


Figure 1. Kaplan-Meier analysis for general survival (A), survival without recurrent myocardial infarction (B), survival without combined endpoint (C) in relation to CHA₂DS₂-VASc and to R₂-CHA₂DS₂-VASc score categories during follow-up

CHA₂DS₂-VASc score was designed for assessing the risk of thromboembolic events in patients with AF [1–3]. It is very simple and broadly known and used by clinicians. Several studies have confirmed the usefulness of this

score in predicting outcomes, including in patients who do not have AF [13–17]. The impact of the CHA₂DS₂-VASc score on clinical outcomes in patients with MI has been reported. In a study on over 13,000 patients with acute

Table III. Effect of components of the (R₂)-CHA₂DS₂-VASc scores on all-cause mortality during full follow-up time available

Parameter	Univariate analysis			Multivariate analysis		
	HR	95% CI	P-value	HR	95% CI	P-value
Age ≥ 65 years	0.79	0.3–1.8	0.59	0.9	0.3–3.0	0.87
Age ≥ 75 years	1.70	1.2–2.4	0.004	1.01	0.6–1.8	0.97
Female gender	1.61	0.8–3.3	0.20	1.07	0.4–2.6	0.87
Heart failure	7.90	3.3–19.0	< 0.001	4.6	1.7–12.0	0.002
Hypertension	0.46	0.2–1.0	0.045	0.39	0.1–1.1	0.07
History of stroke	1.13	0.6–2.0	0.69	0.88	0.4–1.8	0.73
Vascular disease	1.08	0.5–2.2	0.84	1.1	0.5–2.5	0.85
Diabetes	1.82	0.9–3.7	0.10	1.89	0.8–4.5	0.16
GFR ≤ 60 ml/min/1.73 m ²	2.9	1.9–4.5	< 0.001	2.1	1.2–3.6	0.008

GFR – glomerular filtration rate.

Table IV. Receiver operating characteristics analysis of the CHA₂DS₂-VASc and R₂-CHA₂DS₂-VASc scores for predicting clinical events during full follow-up time available

Variable	Cut-off value	Sensitivity	Specificity	AUC	P-value	95% CI
CHA ₂ DS ₂ -VASc:						
All-cause mortality	3	0.67	0.6	0.67	0.003	0.6–0.8
Cardiac mortality	3	0.58	0.58	0.61	0.088	0.5–0.7
All recurrent MI	3	0.71	0.59	0.62	0.11	0.5–0.8
Non-fatal recurrent MI	3	0.69	0.58	0.6	0.17	0.4–0.8
Combined endpoint	3	0.65	0.62	0.64	0.004	0.6–0.7
R ₂ -CHA ₂ DS ₂ -VASc:						
All-cause mortality	4	0.7	0.71	0.76	< 0.001	0.7–0.9
Cardiac mortality	4	0.62	0.69	0.72	< 0.001	0.6–0.8
All recurrent MI	3	0.71	0.51	0.6	0.15	0.5–0.8
Non-fatal recurrent MI	3	0.69	0.51	0.59	0.25	0.4–0.7
Combined endpoint	3	0.79	0.56	0.7	< 0.001	0.6–0.8

MI – myocardial infarction.

coronary syndrome (ACS), those with a high (> 5 points) or intermediate (2–3 points) CHA₂DS₂-VASc score had significantly higher 1-year mortality [7]. In another study on 647 ST-elevation MI patients, those with a CHA₂DS₂-VASc score ≥ 3 had greater in-hospital and 6-month mortality [8]. In 2014, Lau *et al.* showed that CHA₂DS₂-VASc score > 3 is associated with increased risk of ischemic stroke in MI patients [18]. A cut-off value for CHA₂DS₂-VASc score for predicting adverse clinical outcome in the MI population has not been established. In our analysis, the optimal cut-off value for predicting clinical endpoints was 3 for the CHA₂DS₂-VASc score and 4 for the

R₂-CHA₂DS₂-VASc scale. A study conducted by Podolecki *et al.* on 2647 patients with acute MI showed that 1 point increase in the CHA₂DS₂-VASc score is associated with 41% increase in stroke risk and 23% increase in mortality [19]. Some studies suggest even better performance of the CHA₂DS₂-VASc score for predicting cardiovascular events in those patients with MI who do not have AF [20]. Barra *et al.* showed that CHA₂DS₂-VASc score with additional renal function assessment predicts the occurrence of post-discharge ischemic stroke and all-cause mortality in a cohort of patients with MI [21]. A Polish study on over 2000 patients with ACS showed better prognostic

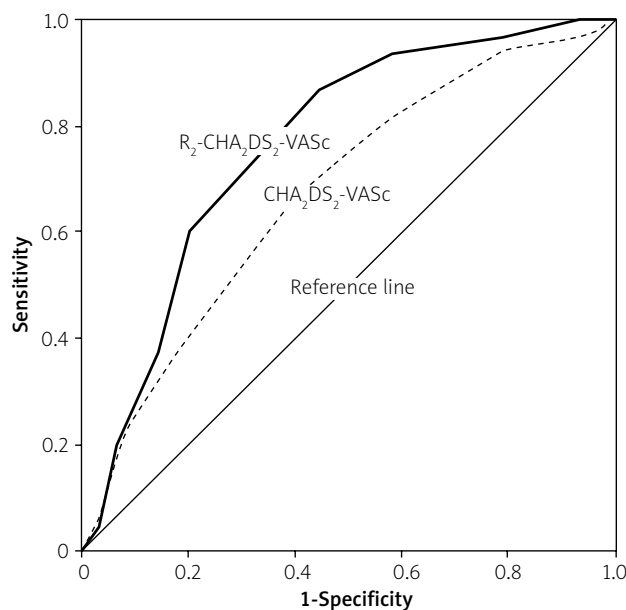


Figure 2. Receiver operating characteristic curves for CHA₂DS₂-VASc and R₂-CHA₂DS₂-VASc scores for predicting all-cause mortality during full follow-up time available

value of the R₂-CHA₂DS₂-VASc score compared to the conventional CHA₂DS₂-VASc scale for predicting all-cause mortality [22]. In our study, ROC analysis showed an AUC value of 0.67 for the CHA₂DS₂-VASc score and 0.76 for the R₂-CHA₂DS₂-VASc score for predicting all-cause mortality.

The CHA₂DS₂-VASc score however has some limitations. It does not take into account several parameters such as cardiac biomarkers or hemodynamic status. On the other hand, all parameters included in the score are established risk factors of adverse clinical outcome in patients with MI [8]. In our analysis, congestive heart failure was associated with the highest hazard ratio for all-cause mortality. Interestingly, a history of arterial hypertension seems to reduce the risk of mortality both in univariate and multivariate analysis (HR < 1). A possible explanation might be less frequent reporting of history of hypertension in patients admitted in a critical condition.

Study limitations

The present study is a retrospective single-center analysis but represents real-world data as consecutive MI patients undergoing primary PCI were enrolled. The sample size was relatively small and the results allow for hypothesis generation only and planning of larger prospective studies. The follow-up was also not completed in 100% of patients, yet the proportion of lacking observations was equal in both groups.

Conclusions

The CHA₂DS₂-VASc score value > 3 points predicts poorer in-hospital and post-discharge outcome in pa-

tients with acute MI undergoing primary PCI. At the same time, patients with a low CHA₂DS₂-VASc score have a good outcome with a relatively small number of events after discharge.

Conflict of interest

The authors declare no conflict of interest.

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